MATERIALS TRANSFER AGREEMENT

Provider:

U.S. Environmental Protection Agency, National Center for Computational Toxicology

Recipient:

CellzDirect Incorporated

1. Provider agrees to transfer to Recipient's Investigator named below the following Research Material:

> A copy of the ToxCast™ chemical library consisting of 50 microliters each of 320 chemical samples prepared as solutions in dimethyl sulfoxide at a concentraton of 20 millimolar.

2. This Research Material may not be used in human subjects. The Research Material will be used only for research purposes by Recipient's investigator in his/her laboratory, for the research project described below, under suitable containment conditions. Recipient agrees to comply with all Federal rules and regulations applicable to the Research Project and the handling of the Research Material.

2(a). Were Research Materials collected according to 45 C.F.R. Part 46, "Protection of Human Subjects?"
____ Yes (Please provide Assurance Number:_____)
____ No
__X__ Not Applicable (Materials not collected from humans)

3. This Research Material will be used by Recipient's investigator solely in connection with the following research project ("Research Project") described with specificity as follows *(use an attachment page if necessary)*:

> CellzDirect, Inc. in collaboration with the EPA may use the research materials provided to investigate and characterize the effects of these compounds on cultures of primary human, mouse, and rat liver cells (e.g. hepatocytes). To this end, CellzDirect, Inc. may examine a variety of endpoints including: mRNA expression assays (e.g. qRT-PCR, RNAse protection), protein expression assays (e.g. Western immunoblotting, ELISA), nuclear receptor activation

assays, transporter assays, and other endpoints such as cell morphology assessments and cytotoxicity assays. These assays/assessments may be performed over multiple concentrations and time points.

Specific examples of the assays that may be run include:
a. Cultures of human hepatocytes and assessing chemical effects on the gene expression profiles of important human enzymes and transporters in high throughput assays capable of highly selective detection of mRNA expression over a large dynamic range of responses. These assays combine sensitive nuclear receptor target genes and probe activators to explore chemical interactions and determine EC50 and Emax values reflective of receptor activation to assess relative potency and efficacy. Correlations of concentration- and time-dependent gene expression profiles with nuclear receptor activation profiles (e.g., example #2 below) would provide a comprehensive view of each chemical's interaction with various master regulators in both an isolated and metabolically competent liver-like environment. These assays have the capability of processing up to 96 chemicals in one 96-well plate of hepatocytes (human) for 16 gene targets simultaneously, but have the flexibility to assess fewer compounds with multiple replicates and dose-response curves for multiple compounds and/or time points, or assessing up to 1300 genes for a single compound on one plate depending on the study design. The most important genes to assay, and how those vary between species would be discussed and agreed upon by the collaborators. This high throughput methodology allows for the rapid assessment of multiple replicates across a range of concentrations and time points simultaneously, using a highly selective and dynamic detection system.
b. Assessing human CAR (hCAR) activation by monitoring its translocation to the nucleus in cultures of primary human hepatocytes. Due to the unique molecular properties of hCAR, gene reporter assays in immortalized cell lines are inadequate to access the activation of hCAR in transformed cell lines. This is also applicable to mouse and rat CAR, however the use of known receptor antagonists for these receptors allows for repression of the high constitutive activity of this receptor followed by de-repression of the antagonist with ligand activators. However, activators such as phenobarbital that activate CAR by translocation can not be modeled in cell lines using any of the immortalized cell systems due to the unique constitutive activity and spontaneous nuclear localization of human and rodent CAR in immortalized cell systems (e.g. HepG2). To effectively assess CAR activation for humans, in vitro assays using immortalized cell lines have been shown not to provide an effective model for predict human CAR activation.

Additionally, some of these compounds may be used in collaborations with the EPA's Virtual Liver program to probe and model the dynamic processes that can occur in mammalian livers and link cell signaling events at the molecular level with liver cell biology phenomena (e.g. cell proliferation). This would mainly involve research in defining and optimizing the conditions required to simulate zone-specific liver toxicity and response to xenobiotic exposure across multiple species in parallel physiology-based model systems to predict human responses. Undefined conditions include ratio of cell types, culture configurations, media conditions, proper assay endpoints and appropriate positive controls responses. These studies may utilize a dynamic flow model system as a new approach to studying these dynamic processes that would simulate a more natural hepatic environment to analyze chemicals in a more relevant system.

4. In all oral presentations or written publications concerning the Research Project, Recipient will acknowledge Provider's contribution of this Research Material unless requested otherwise. To the extent permitted by law, Recipient agrees to treat as confidential, any of Provider's written information about this Research Material that is stamped "CONFIDENTIAL" for a period of five (5) years from the date of its disclosure to recipient. The foregoing shall not apply to information that is or becomes publicly available or which is disclosed to Recipient without a confidentiality obligation. Any oral disclosures from Provider to Recipient which Provider wishes to be treated as confidential shall be identified as being Confidential at the time of the disclosure and by written notice delivered to Recipient within thirty (30) days after the date of the oral disclosure. Recipient may publish or otherwise publicly disclose the results of the Research Project, but if Provider has given Confidential information to Recipient, such public disclosure may be made only after Provider has had thirty (30) days to review the proposed disclosure to determine if it includes any Confidential information, except when the shortened time period is pursuant to a court order or to the extent such review period is permitted by law.

5. The Recipient will provide to the Provider all testing results obtained by the Recipient using the Research Material. Recipient acknowledges that the Provider will make such testing results freely available to the public.

6. This Research Material represents a significant investment on the part of Provider and is considered proprietary to Provider. Recipient's investigator therefore agrees to retain control over this Research Material and further agrees not to transfer the Research Material to other people not under his/her direct supervision without advance written approval of Provider. Provider reserves the right to distribute the Research Material to others and to use it for its own purposes. When the Research Project is

completed, the Research Material will be returned to the Provider or disposed, if directed by Provider.

7. This Research Material is provided as a service to the research community. It is being supplied to Recipient with no warranties, express or implied, including any warranty of merchantability or fitness for a particular purpose. Provider makes no representations that the use of the Research Material will not infringe any patent or proprietary rights of third parties.

8. Recipient shall retain title to any patent or other intellectual property rights in inventions made by its employees in the course of the Research Project. However, if said inventions contain any portion of the Research Material, are derived from the Research Material, or could not have been produced but for the use of the Research Material, Recipient agrees to contact the Provider to determine what ownership interests, if any, the Provider may have, and, where applicable, to negotiate in good faith the terms of a commercial license. Inventorship for a patent application or a commercialized product based on said inventions shall be determined according to United States patent law.

9. When Provider is the EPA: Recipient agrees not to claim, infer, or imply endorsement by the Government of the United States of America (hereinafter referred to as "Government") of the Research Project, the institution or personnel conducting the Research Project or any resulting product(s). Recipient agrees to hold the Government harmless and to indemnify the Government for all liabilities, demands, damages, expenses and losses arising out of Recipient's use for any purpose of the Research Material.

10. When Recipient is the EPA: Provider will not be liable to EPA for any claims or damages arising from EPA=s use of the Research Material.

11. This Agreement shall begin on the date of its execution and continue for twelve (12) months thereafter, and shall automatically renew for successive year long periods (a) unless one party notifies the other party no sooner that thirty (30) days prior to such renewal date that it elects not to renew the Agreement, or (b) unless earlier terminated as provided in the next sentence. The Provider shall have the right to terminate this Agreement at any time if Recipient breaches any of the terms of this Agreement. Upon termination, Recipient shall return to the Provider all unused portions of the Research Materials.

12. All notices pertaining to or required by this Agreement shall be in writing and shall be signed by an authorized representative and shall be delivered by hand (including private courier mail service) or sent by certified mail, return receipt requested, with postage prepaid, addressed as follows.

Provider's Official and Mailing Address:
Robert J. Kavlock, Director
National Center for Computational Toxicology (NCCT)
US EPA (MD-205-01)
4930 Old Page Rd.
Research Triangle Park, NC 27711

Recipient=s Official and Mailing Address:
Edward L. LeCluyse, Chief Scientific Officer
CellzDirect Incorporated
4301 Emperor Blvd.
Durham, NC 27703

13. Paragraphs 2, 6, 8 and 9 shall survive termination.

14. This Agreement shall be construed in accordance with law as applied by the Federal courts in the District of Columbia.

15. The undersigned Provider and Recipient expressly certify and affirm that the contents of any statements made herein are truthful and accurate.